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Application No.10/773,446

Docket No.: 66145(300604)

**AMENDMENTS TO THE SPECIFICATION**

At page 19, please replace the last paragraph comprising a portion of Table 1 with the following amended paragraph:

**Table 1. Human Phagocytosis-related Genes Isolated by CHANGE**

NAME	CLONE NUMBER	NUCLEIC ACID SEQ ID NO.	AMINOACID SEQ ID NO(S)	IDENTITY
PHG-1	6-29	1	<u>71-79</u> <u>70-78</u>	Unknown
PHG-2	33-25	2	<u>80</u> <u>79</u>	Prostaglandin D2 synthase
PHG-3	33-74	3	<u>81</u> <u>80</u>	Myelin basic protein
PHG-4	43-16	4	<u>82-84</u> <u>81-83</u>	Unknown
PHG-5	45-88	5	<u>85</u> <u>84</u>	Unknown

At page 20, please replace the first paragraph with the following amended paragraph, comprising the remainder of Table 1:

PHG-6	53-7	6	<u>86</u> <u>85</u>	Peanut-like 2/septin 4
PHG-7	55-26	7	<u>87</u> <u>86</u>	Coactosin-like 1
PHG-8	55-28	8	<u>88</u> <u>87</u>	Clusterin
PHG-9	57-29	9	<u>89</u> <u>88</u>	Casein kinase 1 epsilon
PHG-10	57-29	9	<u>89</u> <u>88</u>	Casein kinase 1 epsilon (duplicate)
PHG-11	73-51	10	<u>90</u> <u>89</u>	Ferritin heavy polypeptide 1
PHG-12	74-39	11	<u>91</u> <u>90</u>	Metargidin
PHG-13	78-70a	12	<u>92-98</u> <u>91-97</u>	Unknown
PHG-14	78-70c	13	<u>99</u> <u>98</u>	Retinaldehyde binding protein 1
PHG-15	80-31	14	<u>100</u> <u>99</u>	Actin gamma 1

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PHG-16	91-40	15	<u>404100</u>	Matrix metalloproteinase, membrane-associated 1 (MT1-MMP)
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At page 21, please replace the first full paragraph with the following amended paragraph, comprising Table 2:

**Table 2. AMD-Related Phagogenes ("AMDP" Genes) Isolated by Iterative CHANGE Analysis**

NAME	CLONE NUMBER	NUCLEIC ACID SEQ ID NO.	AMINOACID SEQ ID NO(S)	IDENTITY
AMDP-1	33-25	2	<u>8079</u>	Prostaglandin D2 synthase
AMDP-2	37-14	16	<u>402101</u>	SWI/SNF related/OSA-1 nuclear protein
AMDP-3	47-94	17	<u>403-124102- 120</u>	Unknown
AMDP-4	57-29	9	<u>8088</u>	Casein kinase 1 epsilon
AMDP-5	73-51	10	<u>9089</u>	Ferritin heavy polypeptide 1
AMDP-6	91-40	15	<u>404100</u>	Matrix metalloproteinase, membrane associated 1 (MT1-MMP)

At page 21, please replace the last paragraph with the following amended paragraph:

As described above, the invention provides nucleic acid and amino acid sequences relating to genes discovered by a differential cloning strategy (CHANGE) to exhibit altered expression during RPE phagocytosis and/or in AMD. In one aspect, the invention provides novel purified nucleic acids (polynucleotides) isolated by this

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strategy. Previously unknown nucleic acids of the invention include nucleic acid sequences identified herein as PHG-1 (SEQ ID NO:1); PHG-4 (SEQ ID NO. 4); PHG-5 (SEQ ID NO: 5); PHG-13 (SEQ ID NO:12); and AMDP-3 (SEQ ID NO:17). These nucleic acids encode, respectively, polypeptides having the amino acid sequences identified herein as ~~SEQ ID NOS:71-79; 82-84; 85; 92-98; and 103-124~~70-78, 81-83, 84, 91-97, and 102-120.

At page 31, please replace the first paragraph with the following amended paragraph:

**Agents That Modulate Expression or Activity of Phagocytosis-Related and  
AMDP-Related Gene Products**

In another aspect, the invention provides agents that modulate expression levels of mRNA or protein of phagocytosis-related and/or AMDP-related genes. Preferred genes/proteins to be targeted for down-regulation are those showing increased expression in AMD and related disorders, including, as demonstrated herein, prostaglandin D2 synthase, PD2S (respective nucleic acid and amino acid sequences: SEQ ID NOS:2 and ~~80~~79), MT1-MMP (SEQ ID NOS:15 and ~~404~~100) and AMDP-3 (SEQ ID NOS:17 and ~~403-124~~102-120). Preferred genes/proteins to be targeted for up-regulation are those showing decreased expression in AMD and related disorders, including, as demonstrated herein, SWI/SNF related OSA-1 nuclear protein (SEQ ID NOS:16 and ~~402~~101), casein kinase 1 epsilon (SEQ ID NOS:9 and ~~89~~88) and ferritin heavy polypeptide 1 (SEQ ID NOS:10 and ~~404~~89).

At page 40, please replace the second complete paragraph with the following amended paragraph:

Other embodiments of agents that can down-regulate expression or neutralize the biological activity of the phagocytosis-related and/or AMDP-related genes of the invention are based on proteins. An example of a protein that can modulate expression and/or neutralize a biological function of a phagocytosis-related and/or AMDP-related gene product is an antibody that specifically binds a phagocytosis-related and/or AMDP-related polypeptide or peptide. Preferred polypeptides, for which mRNA levels are

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shown herein to be elevated in AMD, include those encoded by nucleic acids having SEQ ID NOS:2, 15 and 17, i.e., polypeptides having amino acid sequences respectively identified herein as SEQ ID NOS:~~8079~~, ~~404100~~, and ~~403-424102-120~~. The antibodies of the invention can be used to interfere with the interaction of a phagocytosis-related and/or AMDP-related protein with one or more molecules that bind or otherwise interact with the phagocytosis-related and/or AMDP-related protein. For instance, an antibody directed against MT1-MMP protein is thought to neutralize the ability of this protein to activate progelatinase A. The results of a study described herein using an antibody directed against MT1-MMP showed delay of retinal degeneration in a rat model of RPE-based disease characterized by over-expression of MT1-MMP. Accordingly, inhibition of excessive production of MT1-MMP in the interphotoreceptor matrix using an anti-MT1-MMP antibody might be used in the eyes of patients with AMD to reduce destruction of the matrix and improve phagocytosis.